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Gene therapy using plasmid DNA encoding vascular endothelial growth factor 164 and fibroblast growth factor 2 genes for the treatment of horse tendinitis and desmitis: Case reports

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Abstract

© 2017 Kovac, Litvin, Aliev, Zakirova, Rutland, Kiyasov and Rizvanov. In this clinical study, for the first time we used the direct gene therapy to restore severe injuries of the suspensory ligament branch and superficial digital flexor tendon in horses (Equus caballus). We injected the plasmid DNA encoding two therapeutic species-specific growth factors: vascular endothelial growth factor 164 and fibroblast growth factor 2 at the site of injury in the suspensory ligament branch and tendon. Treatment effects were evaluated with the use of clinical observation and ultrasound imaging during a period of a few months. We showed that gene therapy used within a period of 2-3 months after the injury resulted in the complete recovery of functions and full restoration of the severely damaged suspensory ligament and superficial digital flexor tendon.

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Keywords

Fibroblast growth factor, Gene therapy, Horse, Suspensory ligament, Tendon, Vascular endothelial growth factor

References

[1] Kovac M, Nowak M, Küpers S, Tambur Z. Frequency of orthopedic diseases in horses: a retrospective study. Vet Glas (2002) 56:307-19. doi:10.2298/VETGL0206307K

[2] Riley G. The pathogenesis of tendinopathy. A molecular perspective. Rheumatology (2004) 43:131-42. doi:10.1093/rheumatology/keg448

[3] Clegg PD, Strassburg S, Smith RK. Cell phenotypic variation in normal and damaged tendons. Int J Exp Pathol (2007) 88:227-35. doi:10.1111/j.1365-2613.2007.00549.x

[4] Kearney RS, Parsons N, Metcalfe D, Costa ML. Injection therapies for achilles tendinopathy. Cochrane Database Syst Rev (2015) 5:1-78. doi:10.1002/14651858.CD010960.pub2

[5] Uysal CA, Tobita M, Hyakusoku H, Mizuno H. Adipose-derived stem cells enhance primary tendon repair: biomechanical and immunohistochemical evaluation. J Plast Reconstr Aesthet Surg (2012) 65:1712-9. doi:10.1016/j.bjps.2012.06.011

[6] Middleton KK, Barro V, Muller B, Terada S, Fu FH. Evaluation of the effects of platelet-rich plasma (PRP) therapy involved in the healing of sports-related soft tissue injuries. Iowa Orthop J (2012) 32:150-63

[7] Martinek V, Huard J, Fu FH. Gene therapy in tendon ailments. Tendon Inj Basic Sci Clin Med (2005). p. 307-12. doi:10.1007/1-84628-050-8_30

[8] Litvin YA, Zakirova EY, Zhuravleva MN, Rizvanov AA. Generation of plasmid DNA expressing species-specific horse VEGF164 and FGF2 factors for gene therapy. Bionanoscience (2016) 6:550-3. doi:10.1007/s12668-01--0273-2

[9] FDA. Considerations for Plasmid DNA Vaccines for Infectious Disease Indications. USA: Food and Drug Administration (2007). p. 1-18

[10] FDA. Content and Review of Chemistry, Manufacturing, and Control (CMC) Information for Human Somatic Cell Therapy Investigational New Drug Applications (INDs). USA: Food and Drug Administration (2008). p. 1-89

[11] EMA. Reflection Paper on Design Modifications of Gene Therapy Medicinal Products during Development. London: European Medicines Agency (2001). p. 1-9

[12] EMA. Guideline on the Non-Clinical Studies Required before First Clinical Use of Gene Therapy Medicinal Products. London: European Medicines Agency (2008). EMEA/CHMP/GTWP/125459/2006

[13] Zakirova EY, Vasin NN, Zhuravleva MN, Rizvanov AA. Case report of application gene construction with VEGF and BMP2 in restoration of tear in the anterior cruciate ligament of a large breed dog. Genes Cells (2014) 9:93-5

[14] Plotnikov MV, Rizvanov AA, Masgutov RF, Mavlikeev MO, Salafutdinov II, Gazizov IM, et al. The first clinical experience of direct gene therapy using VEGF and bFGF in treatment patients with critical lower limb ischemia. Cell Transplant Tissue Eng (2012) 7:180-4

[15] Evans CH, Ghivizzani SC, Robbins PD. Orthopedic gene therapy in 2008. Mol Ther (2009) 17:231-44. doi:10.1038/mt.2008.265

[16] Tang JB, Wu YF, Cao Y, Chen CH, Zhou YL, Avanessian B, et al. Basic FGF or VEGF gene therapy corrects insufficiency in the intrinsic healing capacity of tendons. Sci Rep (2016) 6:20643. doi:10.1038/srep20643

[17] Byrne AM, Bouchier-Hayes DJ, Harmey JH. Angiogenic and cell survival functions of vascular endothelial growth factor (VEGF). J Cell Mol Med (2005) 9:777-94. doi:10.1111/j.1582-4934.2005.tb00379.x

[18] Deev R, Plaksa I, Bozo I, Isaev A. Results of an international postmarketing surveillance study of pl-VEGF165 safety and efficacy in 210 patients with peripheral arterial disease. Am J Cardiovasc Drugs (2017) 17(3):235-42. doi:10.1007/s40256-016-0210-3

[19] Deev RV, Bozo IY, Mzhavanadze ND, Voronov DA, Gavrilenko AV, Chervyakov YV, et al. pCMV-vegf165 intramuscular gene transfer is an effective method of treatment for patients with chronic lower limb ischemia. J Cardiovasc Pharmacol Ther (2015) 20:473-82. doi:10.1177/1074248415574336